REMARKS

Upon entry of the present amendment, claims 29, 31, 33-36, 39-43, 45-47, 51-52, 54, and 56 are pending in the application. Claims 30, 32, 44, 48-50, 53, 55, and 57-58 were canceled, and claims 29, 31, 33, 34, 39-41, 45-47, 52, and 54 were amended. The amendments to independent claims 29, 33, 34 are supported by disclosure at page 5, lines 14-16, of the specification. Claims 31, 39, and 45 were amended to add reference to an antibody-producing hybridoma cell line, which was deposited with the American Type Culture Collection (ATCC). The remaining claim amendments were made to correct typographical errors and claim dependency.

The specification has been amended to clarify that HAAH polypeptide refers to the amino acid sequence of SEQ ID NO:2 and HAAH cDNA refers to the nucleotide sequence of SEQ ID NO3. The claims have also been amended accordingly. The specification has also been amended to insert a reference to a sequence (SEQ ID NO:2) on page 6, line 16.

With respect to the Declaration/ Power of Attorney, co-inventor, Dr. Carlson, has initialed and dated the correction of his home address. An initialed/dated copy of the Combined Declaration and Power of Attorney document is submitted herewith.

No new matter has been added by this amendment.

35 U.S.C. § 112, second paragraph

Claims 29, 30, 33-36, 42, 43, 48, 51, 52, 56, and 57 were rejected for indefiniteness for recitation of "HAAH" as the only means of identifying a protein to which the claimed antibodies bind. As requested by the examiner, the pending claims have been amended to insert a sequence identifier.

35 U.S.C. § 112, first paragraph

Claims 31, 32, 39, 40, 41, 44-47, 50, 53-55, and 58 were rejected for lack of enablement.

Claims 32, 44, 50, 53, and 58 were canceled. The remaining claims have been amended to identify an antibody-producing hybridoma cell line, which was deposited with the ATCC. A copy of the ATCC deposit receipt is submitted herewith.

Claims 29, 30, 33-36, 42, 43, 48, 49, 51, 52, 56, and 57 were rejected for lack of written description. Independent claims 29, 33, and 34 were amended to require that the antibody bind to an epitope of within 650 to 700 of SEQ ID NO:2. In view of the amendment, this rejection can now be withdrawn.

Claims 33, and 45-52 were rejected for lack of enablement. Claim 33 has been amended to require a composition, which includes a monoclonal antibody that binds to an epitope within a catalytic domain of HAAH (SEQ ID NO:2) linked to a cytotoxic agent that preferentially kills tumor cells compared to non-tumor cells, as suggested by the Examiner. In view of the present amendment, Applicant submits that this ground of rejection is moot.

35 U.S.C. § 102

Claims 29 and 43 were rejected for anticipation by Radosevich et al. as evidenced by Radosevich (USPN 6,166,176; "the 176 patent"). Claim 43 was canceled, and claim 29 was amended to require binding to an epitope within amino acids 650-700 of SEQ ID NO:2. Neither of the Radosevich references describe an antibody that binds to the required domain of HAAH (SEQ ID NO:2) now required by the claims.

Claims 29, 33, 43, and 49 were rejected for anticipation by Sinkule et al. as evidenced by Radosevich (the '176 patent) and the abstract of Tomida at al. The amended claims are novel over the cited art. Both Sinkule and Radosevich describe monoclonal antibody 44-3A6, which binds to residues 117-123 of labyrinthin (corresponding to residues 175-181 of HAAH). Claims 29 and 33 require that the claimed monoclonal antibody bind to an epitope within residues 650-

700 of SEQ ID NO:2, a domain that is not present in labyrinthin. Therefore, the amended claims are not anticipated by Sinkule et al.

Claims 29, 43, and 44 were rejected for anticipation by Lavaissiere et al. As was discussed above, claims 43 and 44 were canceled. Claim 29 was amended to require antibody binding to a specific epitope region of HAAH (residues 650-700 of SEQ ID NO:2). Such a binding specificity is not described by Lavaissiere et al. Therefore, this rejection should be withdrawn.

Claims 29 and 42 were rejected for anticipation by Carter et al. Amended claim 29 recites a monoclonal antibody that binds to an epitope within carboxy-terminal residues 650-700 of SEQ ID NO:2, whereas the antibodies of Carter bind to sequences, which may correspond to certain amino-terminal sequences of SEQ ID NO:2. The amended claims are therefore novel over Carter et al.

Applicants submit that the claims as now amended are not anticipated by the cited art and respectfully request withdrawal of the rejections for anticipation.

35 U.S.C. § 103

Claims 29, 34-36, 42, 43, 56, and 57 were rejected for obviousness over Radosevich et al. as evidenced by the '176 patent in view of Wels et al. and Schlom et al. The amended claims are nonobvious over the cited art, because neither of the Radosevich prior art references describe an antibody that binds to residues 650-700 of SEQ ID NO:2. The binding specificity is not provided by any of the secondary references, i.e., the Wels and Schlom references also fail to describe the HAAH domain now required by the amended claims. Therefore, this combination of references does not suggest the claimed invention.

Claims 29, 33, 42, 43, 48, and 49 were rejected for obviousness over Sinkule et al. as evidenced by the '176 patent and the abstract of Tomida et al. for the reasons set forth in the Examiner's rejection for anticipation by Sinkule et al. (section 14 of the Office Action). Sinkule et al. describe a specific monoclonal antibody, which binds to an epitope far removed from residues 650-700 of SEQ ID NO:2. Neither Sinkule et al. nor the '176 patent describe an epitope or HAAH domain defined by the amended claims. Tomida et al. describe drug resistance in tumor cells and also fail to provide any sequence information lacking in Sinkule. In view of the amendment of claim 29 (requiring that the antibody bind to an epitope within residues 650-700 of SEQ ID NO:2), Applicants submit that the amended claims are non-obvious over the cited combination of references.

Claims 29, 30, 43, and 44 were rejected for obviousness over Lavaissiere et al. in view of Goding and the '176 patent. The Examiner states:

> One of skill in the art would have been motivated to make a specific antibody which would bind to the carboxyl terminus of HAAH to avoid cross reactivity to Labyrinthin, and attain an accurate measurement of the amount of HAAH protein in a sample, as levels of Labyrinthin would not be correlated with hydroxylation.

Lavaissiere et al. fail to describe or suggest the specific region (residues 650-700 of SEQ ID NO:2) required by the amended claims. The '176 patent fails to describe such a sequence, because the protein described by the '176 patent is a splice variant that lacks a sequence defined by residues 650-700 of SEQ ID NO:2. Goding is a general reference from nearly twenty years ago, which describes the advantages of monoclonal antibodies compared to antisera. This combination in no way suggests a monoclonal antibody with the precise binding specificity required by the amended claims. Moreover, neither reference makes any mention at all of a

reason or need to distinguish HAAH from Labyrinthin; therefore, there is no motivation to make the antibody now defined by the amended claims.

Double Patenting

Claims 29, 31, 39, 43, 44 and 34, 57, and 58 were provisionally rejected for obviousness-type double patenting over claims 35 and 39-43 of copending application USSN 09/859,604 (the '604 application) in view of Lavaissiere et al. The '604 application is a continuation-in-part of the present application. Neither the cited claims of the '604 application nor Lavaissiere describe the antibody that binds to residues 650-700 of SEQ ID NO:2; therefore, the rejection of claims 29 and 34 should be withdrawn. With respect to claims 31 and 39, Applicants will file a terminal disclaimer (if still applicable), upon notification of allowable claims.

Claims 29, 31, 34-36, 39-44 and 53-58 were rejected for obviousness-type double patenting over claims 35 and 39-43 of the '604 application in view of Lavaissiere et al. and Schlom. As was discussed above, neither the claims of the '604 application nor the cited literature describe or suggest the binding specificity now required by claims 29 and 34 (and those claims depending therefrom). With respect to the remaining claims, a terminal disclaimer (if still applicable) will be filed upon notification of allowable claims in the present application.

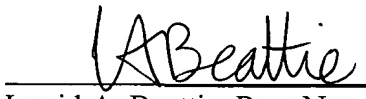
CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested.

A petition for extension of time and a check in the amount of $2010 is enclosed to cover the petition fee for a five (5) month extension of time pursuant to 37 C.F.R. § 1.17(a)(3). The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21486-032DIV5.

Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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